

Claims

1. Method for manufacture of sertindole comprising manufacturing 5-chloro-1-(4-fluorophenyl)-indole and converting it to sertindole characterised in that the method
 5 for manufacture of 5-chloro-1-(4-fluorophenyl)-indole comprises reacting 5-chloro-indole with a 4-fluorophenylhalide in the presence of a base, a chelating ligand and catalytic amounts of a copper salt comprising copper(I) or copper(II) and an anion which does not interfere in an unfavourable way with the reaction.
- 10 2. Method for manufacture of 5-chloro-1-(4-fluorophenyl)-indole comprising reacting 5-chloro-indole with a 4-fluorophenylhalide in the presence of a base, a chelating ligand and catalytic amounts of a copper salt comprising copper(I) or copper(II) and an anion which does not interfere in an unfavourable way with the reaction.
- 15 3. Method according to claim 1 or 2 characterised in that the chelating ligand is a substituted or unsubstituted 1,10-phenanthroline or a compound of the formula $X-(CR^1R^2-(CR^5R^6)_n-CR^3R^4-Y)_m$, wherein X and Y independently are selected from NR^7R^8 and OR^9 , R^1 - R^9 independently are selected from hydrogen, C_{1-6} -alkyl, C_{1-6} -alkyl carboxylic acid and aryl or one of R^1 and R^2 together with one of R^5 and R^6 are C_{3-6} -alkylene, m is 1 or 2 and n is
 20 0, 1, 2 or 3.
4. Method according to claim 3 characterised in that the chelating ligand is selected from the group comprising 1,2-cyclohexanediamine, N,N,N,N-tetramethyl ethylenediamine, N,N-diethyl ethylenediamine, ethylenediamine, ethylenediamine N,N,N,N-tetraacetic acid
 25 (EDTA), diethylenetriamine N,N,N,N,N-pentaacetic acid (DTPA) and substituted or unsubstituted 1,10-phenantroline, typically the chelating ligand is selected from 1,2-cyclohexanediamine, N,N,N,N-tetramethyl ethylenediamine, N,N-diethyl ethylenediamine and ethylenediamine, in particular the chelating ligand is ethylenediamine.
- 30 5. Method according to any one of claims 1-4 characterised in that the copper salt is selected from CuCl, CuBr, CuI, CuCl₂, CuBr₂, CuI₂, CuOCOCH₃, Cu(OCOCH₃)₂, anhydrous or hydrated CuSO₄, CuCO₃, Cu₂O and mixtures of said copper salts, typically the copper salt is selected from CuCl, CuBr, CuI, CuCl₂, CuBr₂ or CuI₂.

6. Method according to any one of claims 1-5 characterised in that the 4-fluorophenylhalide is selected from 4-fluoro-bromobenzene or 4-fluoro-iodobenzene, such as 4-fluoro-bromobenzene.
- 5 7. Method according to any one of claims 1-6 characterised in that the 4-fluorophenylhalide is added in a molar surplus relative to the 5-chloro-indole.
8. Method according to claim 7 characterised in that the molar surplus is in the range from 1.1 to 3.
- 10 9. Method according to any one of claims 1-8 characterised in that the catalytic amounts of the copper salt is less than 20 mol % relative to the 5-chloro-indole, typically less than 10 mol % relative to the 5-chloro-indole, such as in the range from about 1 to about 5 mol %.
- 15 10. Method according to any one of claims 1-9 characterised in that the base is selected from the carbonates, hydrogen carbonates, phosphates, hydrogen phosphates, dihydrogen phosphates, oxides and hydroxides of alkali metals.
11. Method according to claim 10 characterised in that the base is present in a molar excess
20 relative to the 5-chloro-indole, typically the amount of base is in the range from about 1.05 molar equivalents to about 2.5 molar equivalents.
12. Method according to any one of claims 1-11 characterised in that reaction is completed at
25 temperatures in the range from above 80 °C to 200 °C, typically in the range from 100 °C to 160 °C.